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Author manuscript

Coron Artery Dis. Author manuscript; available in PMC 2015 September 22.

Published in final edited form as:

Coron Artery Dis. 2014 December ; 25(8): 698–704. doi:10.1097/MCA.0000000000000150.

Correlation between coronary artery calcium score and aortic diameter in a high-risk population of elderly male hypertensive patients

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Abstract

Background—Studies on the relationship between coronary artery calcium and aortic diameter are scarce. The aim of the current study was to evaluate the correlation between coronary artery calcium score (CACS) and maximal thoracic and abdominal aortic diameters in a population of elderly (>65 years) male hypertensive patients at high risk for coronary artery disease.

Patients and methods—From June 2012 to April 2013, we prospectively enrolled 393 male hypertensive patients older than 65 years of age who had no history of aortic aneurysm. Coronary artery calcium and maximal diameters of the ascending thoracic aorta (ATA_{max}), descending thoracic aorta (DTA_{max}), and abdominal aorta (AA_{max}) were measured using noncontrast computed tomography imaging. Aortic diameters are indexed to body surface area (BSA). Participants were divided into five groups according to CACS (0, 1–10, 10–100, 100–400, and > 400).

Results—The mean ATA_{max}/BSA, DTA_{max}/BSA, and AA_{max}/BSA were 22.0 ± 2.7 , 16.3 ± 1.9 , and 13.0 ± 2.9 mm, respectively. On multivariate analysis, ATA_{max}/BSA was associated independently with age, diabetes, and history of aortic valve replacement (all $P < 0.001$). DTA_{max}/BSA was associated independently with age ($P < 0.001$). However, there were no significant correlations between thoracic aorta diameter and CACS. In contrast, AA_{max}/BSA was associated independently with CACS as well as age and history of smoking ($P = 0.014$, 0.003 , and

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Conflicts of interest

There are no conflicts of interest.

0.019, respectively). Abdominal aortic aneurysm (>30 mm) was more prevalent in patients with a CACS of 400 or more compared with the others (14 vs. 3%, $P < 0.001$).

Conclusion—CACS was associated with increased abdominal aorta diameter, but not with thoracic aorta diameter. Therefore, screening for an abdominal aortic aneurysm is warranted in patients with a high risk of coronary artery disease and a high CACS. However, the necessity for thoracic aortic aneurysm screening is not clear in these patients.

Keywords

aneurysm; aorta; coronary artery calcium

Introduction

Early detection of an aortic aneurysm is important in patients at high risk because of its life-threatening potential. These aneurysms are typically asymptomatic until rupture, which can be catastrophic; therefore, reliable screening for patients at risk is critical [1]. Some studies have reported that abdominal aortic (AA) aneurysms are more prevalent in patients undergoing cardiac catheterization for coronary artery disease (CAD) or awaiting coronary artery bypass grafting [2,3]. As both conditions share common risk factors and pathophysiological substrates [4], we hypothesized that there is an association between AA aneurysm and CAD. Ascending thoracic aortic (ATA) aneurysms have a different etiology from AA aneurysms and most often result from cystic medial degeneration [1]. This process occurs normally to some extent with aging and is accelerated by hypertension [5], both of which are known risk factors for CAD. However, the relationship between CAD and thoracic aortic aneurysm has not been clearly defined.

It has been reported that coronary artery calcium is strongly related to the presence of coronary atherosclerotic plaques [6,7], and a high coronary artery calcium score (CACS) on screening computed tomography (CT) in an asymptomatic person portended a very high risk for coronary events [8]. Therefore, CACS measured on a screening noncontrast CT has been used widely to identify patients at high risk for CAD in asymptomatic populations [9].

Coronary artery calcification and aortic aneurysm share similar risk factors including advanced age and hypertension, and they both require screening in asymptomatic patients. In addition, they can be obtained simultaneously using a noncontrast CT scan. However, data on the relationship between CACS and aortic diameter are scarce. Therefore, our aim was to determine whether CACS correlates with aortic diameter in elderly male patients with hypertension, who are at high risk for atherosclerosis and CAD.

Patients and methods

Study population

We prospectively enrolled 542 consecutive patients from June 2012 to April 2013 at the outpatient clinic of Severance Cardiovascular Hospital (Seoul, Republic of Korea). All patients were male hypertensive patients older than 65 years of age without a history of aortic aneurysm. We excluded 30 patients with suboptimal CT images and 119 patients with

a history of coronary artery stent revascularization in whom an accurate CACS could not be calculated because of the presence of coronary stents. The remaining 391 patients comprised the study population. This study was approved by our institutional review board and informed consent was obtained from all patients.

Measurement of clinical variables

Data on a history of hypertension, diabetes, smoking, and aortic valve replacement (AVR) were obtained from medical records. Height, weight, and blood pressure were measured during the initial patient visit. Serum calcium, phosphorus, total cholesterol, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, triglyceride, and serum creatinine level were measured after a minimum 12-h fasting period. Hypertension was defined as systolic blood pressure 140 mmHg or more and/or diastolic blood pressure 90 mmHg or more or treatment with antihypertensive agents. Diabetes was defined as treatment with hypoglycemic agents or insulin, or fasting glucose 126 mg/dl or more. Dyslipidemia was defined as any one of the following: total cholesterol 240 mg/dl or more, low-density lipoprotein-cholesterol 130 mg/dl or more, high-density lipoprotein-cholesterol 40 mg/dl or less, triglyceride 150 mg/dl or more, and/or treatment with lipid-lowering agents. Ever-smoking was defined as having smoked for more than 1 year.

Computed tomography imaging protocol and analysis

All examinations were performed on a 320-row CT system (Aquilion ONE; Toshiba Medical Systems, Otawara, Japan) with patients positioned supine on the table. Dual scanograms were used for planning the examination and determining the anatomical range to be covered. Multiple volumes were placed to cover the entire aorta from above the aortic arch to the aortic bifurcation. Patients underwent aortic CT with a prospective ECG-gating wide-volume protocol (from four to six volumes, according to body height). Data were obtained from 40 to 50% of the R–R interval. The CT gantry rotation time was 350 ms. The tube voltage was 120 kV and the effective tube current was adjusted using the adaptive iterative dose reduction three-dimensional (AIDR 3D) algorithm. The resulting four to six individual volume data sets were automatically stitched together immediately after reconstruction to generate one CT data set of the entire aorta. All data were reconstructed using a standard soft-tissue and lung kernel (FC43). Images were reconstructed with a slice thickness of 0.5 mm. The CT angiography data sets were reconstructed at 45% of R–R intervals. CACS acquisition was performed in a single gantry rotation during breath hold at inspiration, which allows image reconstruction at a single cardiac phase. The tube voltage was 120 kV and the effective tube current was adjusted using the AIDR 3D algorithm.

Systemic measurements of the ascending and descending thoracic aorta (ATA_{PAB} and DTA_{PAB}) were performed at the outer aortic wall perpendicular to the axis of the aorta in the axial plane at the lower level of the pulmonary artery bifurcation (Fig. 1a). After measuring ATA_{PAB} and DTA_{PAB} , maximal ascending thoracic aorta diameter (ATA_{max}) was measured in the axial plane from just above the aortic root to the aortic arch perpendicular to the axis of the aorta. Similarly, the maximal descending thoracic aorta diameter (DTA_{max}) was measured at the descending thoracic aorta (DTA) distal from the aortic arch to the diaphragm level of the thoracic aorta in the same axis. We reassessed

ATA_{max} and DTA_{max} in the sagittal and coronal planes using reconstructed images (Fig. 1c and d) to avoid slicing through the aorta off-axis, which would result in a falsely large diameter [1]. Aortic diameter at the superior mesenteric artery (AA_{SMA}) was measured at the first slice inferior to the origin of the superior mesenteric artery in the axial plane (Fig. 1b). Maximal abdominal aortic diameter (AA_{max}) was defined as the maximal diameter of the AA from the diaphragm to the first slice superior to the aortic bifurcation. Aortic diameters were indexed to body surface area (BSA).

Coronary scans were used to identify each focus of calcification with a minimal density of 130 HU and a minimal voxel size of 1.03 mm³ along the course of the coronary artery. For each calcified focus, a score was calculated according to the volume score methods. The volume score was calculated using the interpolation method described by Callister *et al.* [11]. The volume score measures the volume of the calcium by the density factor. The sum of all patient scores constituted the total CACS. Participants were categorized on the basis of the CACS in the following manner: CACS = 0, 0 < CACS ≤ 10, 10 < CACS ≤ 100, 100 < CACS ≤ 400, and CACS > 400.

Statistical analysis

The distribution for all relevant variables was reported either as a percentage or as the mean ± SD. The groups were compared using χ^2 statistics for categorical variables. One-way analysis of variance was used to compare the differences in aortic diameters according to the CACS. To determine independent correlates of maximal aortic diameters, linear relationships were assessed by simple linear regression analysis. Variables with a *P*-value less than 0.2 on univariate analysis were entered into the multiple linear regression model. A *P*-value of less than 0.05 was considered statistically significant.

Results

The demographic and clinical characteristics of all patients enrolled in this study are shown in Table 1. The mean age of the patients was 73 years. Diabetes and dyslipidemia were diagnosed in 30 and 58% of the patients, respectively, and ~70% had a history of smoking. The mean ATA_{max}/BSA, DTA_{max}/BSA, and AA_{max}/BSA were 22.0 ± 2.7, 16.3 ± 1.9, and 13.0 ± 2.9 mm, respectively. Aortic diameters according to CACS are shown in Table 2. There were no significant differences in ATA_{PAB}/BSA, ATA_{max}/BSA, DTA_{PAB}/BSA, and DTA_{max}/BSA among the CACS groups. However, AA_{SMA}/BSA and AA_{max}/BSA increased significantly as the CACS increased (*P* for trend = 0.017 and 0.002, respectively). Figure 2 shows the individual ATA_{max}/BSA, DTA_{max}/BSA, and AA_{max}/BSA values in the study population. Most patients (55/56, 98%) with a CACS of 0 had an AA_{max} of 30 mm or less, with the exception of one patient, who had an AA_{max} of 40 mm.

Figure 3 shows the prevalence of abdominal aortic aneurysm according to the CACS. On the basis of a reported maximum diameter of 20mm of normal infrarenal aorta, AA aneurysm is more commonly defined as a maximum diameter of greater than 30 mm [12]. When patients were categorized into two groups (CACS ≤ 400 and CACS > 400), abdominal aneurysm (AA_{max} > 30 mm) [12] was more prevalent in patients with a CACS of 400 or more (14 vs.

3%, $P < 0.001$). However, the overall prevalence of AA aneurysm 50–59 mm was low (0.5%, 2/393) and all belonged to the CACS more than 400 group.

Table 3 shows the results of the regression analysis of variables for determinants of maximal aorta diameters. On multivariate analysis, ATA_{max}/BSA diameter was associated independently with age, diabetes, and a history of AVR (all $P < 0.001$), and DTA_{max}/BSA was associated independently with age ($P < 0.001$). However, there were no significant correlations between thoracic aortic diameters and CACS. In contrast, AA_{max}/BSA was associated independently with CACS, as well as age and history of smoking ($P = 0.014$, 0.003, and 0.019).

Discussion

The principal findings of the current study are that (i) CACS was associated with increased AA diameter, but not with the diameters of the ATA and DTA, and (ii) the prevalence of AA aneurysm was greatest in patients with a CACS of 400 or more.

Arterial calcium development is strongly associated with vascular injury and atherosclerotic plaque formation [13]. The prevalence of coronary artery calcium reflects the prevalence of coronary atherosclerosis, and calcification of the coronary arteries occurs in approximate proportion to the severity and extent of coronary atherosclerosis [14]. According to a meta-analysis by Pletcher *et al.* [15], the risk of major CAD events increases 2.1-fold and 10-fold for scores ranging from 1–100 to 400, respectively, as compared with scores of 0. Therefore, noncontrast CT screening for detection of CACS is currently recommended in asymptomatic intermediate-risk patients and low-risk patients with a family history of premature coronary heart disease to assess the burden of coronary atherosclerosis [9].

From the current study, we found that CACS was significantly associated with AA diameter, as we hypothesized on the basis of the common pathophysiology of coronary calcification and AA aneurysm. Patients with a CACS over 400 had an AA aneurysm prevalence up to 14%, which was much higher than that in other patients (3%). CAD and AA aneurysm share many of the same atherosclerotic risk factors, although their causes are diverse. Several previous studies have addressed the relationship between CAD and AA aneurysm. Significant CAD was found in 33% of patients who were already scheduled for surgical correction of an AA aneurysm [16]. The prevalence of AA aneurysm was 14% in elderly patients with CAD, which was much higher than that in age-matched controls (3%) [4]. The present study population included male hypertensive patients older than 65 years of age who were at high risk for CAD. More than 70% had a history of smoking more than 1 year in their lifetime. However, the overall prevalence of AA aneurysm, which has been reported to be associated with a high annual rupture risk of 6.5% [17], was very low (0.5%) and patients with a high rupture risk (AA aneurysm diameter of 50–59 mm) all belonged to the CACS of 400 or more subgroup. These findings suggest that screening of the AA to rule out aneurysm might be worth considering in patients with CACS of 400 or more who have a high CAD risk.

Although aging and hypertension are also known common risk factors for both ATA aneurysm and atherosclerosis, there were no differences in ATA and DTA among the CACS groups. Cystic medial degeneration, the pathophysiology of aneurysm, and dilation of the ATA is associated with the aging process and is known to be accelerated by hypertension [5]. Nevertheless, CACS, which reflects coronary atherosclerosis, was not associated with thoracic aorta dilation in the current study.

This result is consistent with the notion that, in contrast to AA aneurysms, ATA aneurysms are not considered to be the result of atherosclerosis [18], and they are usually a clinical component of heritable connective tissue disorders such as Marfan syndrome, Ehlers–Danlos syndrome, and bicuspid aortic valve [19,20].

In this study, 3.8% of patients had a history of AVR, and AVR was an independent determinant of ATA diameter in addition to age and BSA. Patients who undergo AVR are often reported to have some degree of ascending aortic dilation because of poststenotic aortic dilation or aortic regurgitation [21], but the natural history of ATA dilation following AVR is not certain. The incidence of aortic valve disease is increasing worldwide because of the aging population [22]. Optimal screening strategies for ATA aneurysms in elderly patients with aortic valve disease should be discussed in further studies.

Limitations

The data comprise a population of elderly male patients with hypertension, and therefore the results cannot directly be applied to low-risk populations or women. Measurement of aortic diameter by noncontrast CT in the transverse plane may not be representative of the true short axis; thus, a contrast CT study may be required. However, we reassessed our measurements in the sagittal and coronal planes using reconstructed images to avoid slicing through the aorta off-axis. The prevalence of smoking history was high in the population studied and the current guidelines recommend that elderly male patients with a smoking history have an indication for AA aneurysm screening. Therefore, the vast majority of patients should be screened irrespective of CACS. However, as CACS showed a significant correlation even after adjusting for smoking history, further large studies in a population of low smoking prevalence would help to clarify the association between CACS and AA aneurysm. Aortic volume would be more reliable than diameter as it has been reported that in patients with untreated aortic aneurysm, a change in aortic volume could occur in the absence of a significant change in maximal diameter [23]. Therefore, further studies using aortic volume would be more helpful to define the precise relation between CACS and aortic size.

Conclusion

CACS was associated with increased AA diameter, but not with the ATA and DTA. Screening of the AA to rule out an aneurysm might be worth considering in patients at high risk of CAD who have a CACS more than 400. However, the necessity for thoracic aortic aneurysm screening is not clear in those patients.

Acknowledgements

This research was supported by the Leading Foreign Research Institute Recruitment Program through the National Research Foundation of Korea (NRF), funded by the Ministry of Science, ICT & Future Planning (MSIP) (no. 2012027176).

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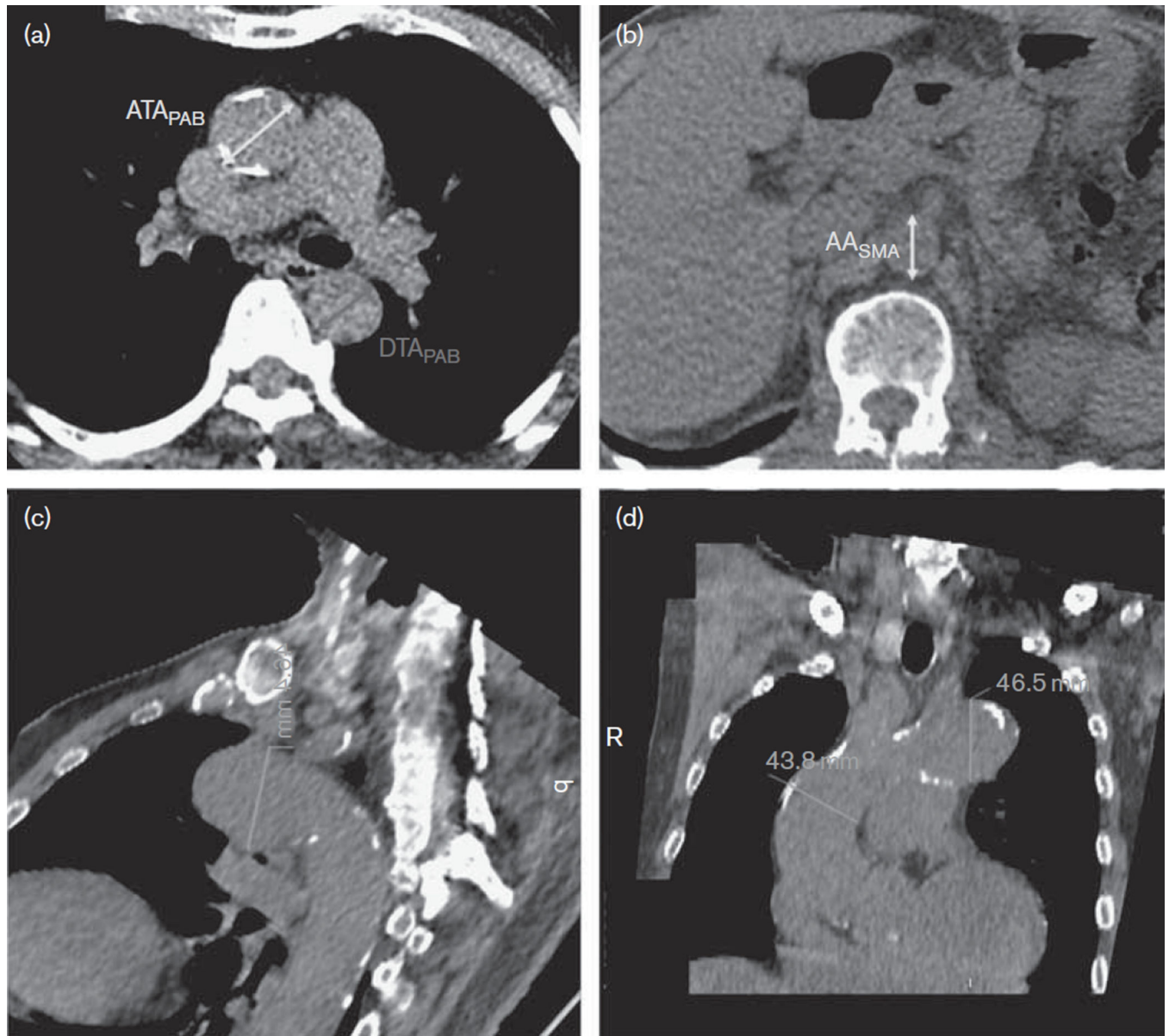


Fig. 1. Measurement of aortic diameters. (a) Ascending and descending thoracic aorta at the pulmonary artery bifurcation (PAB) and (b) abdominal aorta at the superior mesenteric artery (SMA) in the axial plane. The maximal diameter of ascending and descending thoracic aorta was remeasured in the sagittal (c) and coronal planes (d) using reconstructed images [10]. AA, abdominal aorta; ATA, ascending thoracic aorta; DTA, descending thoracic aorta.

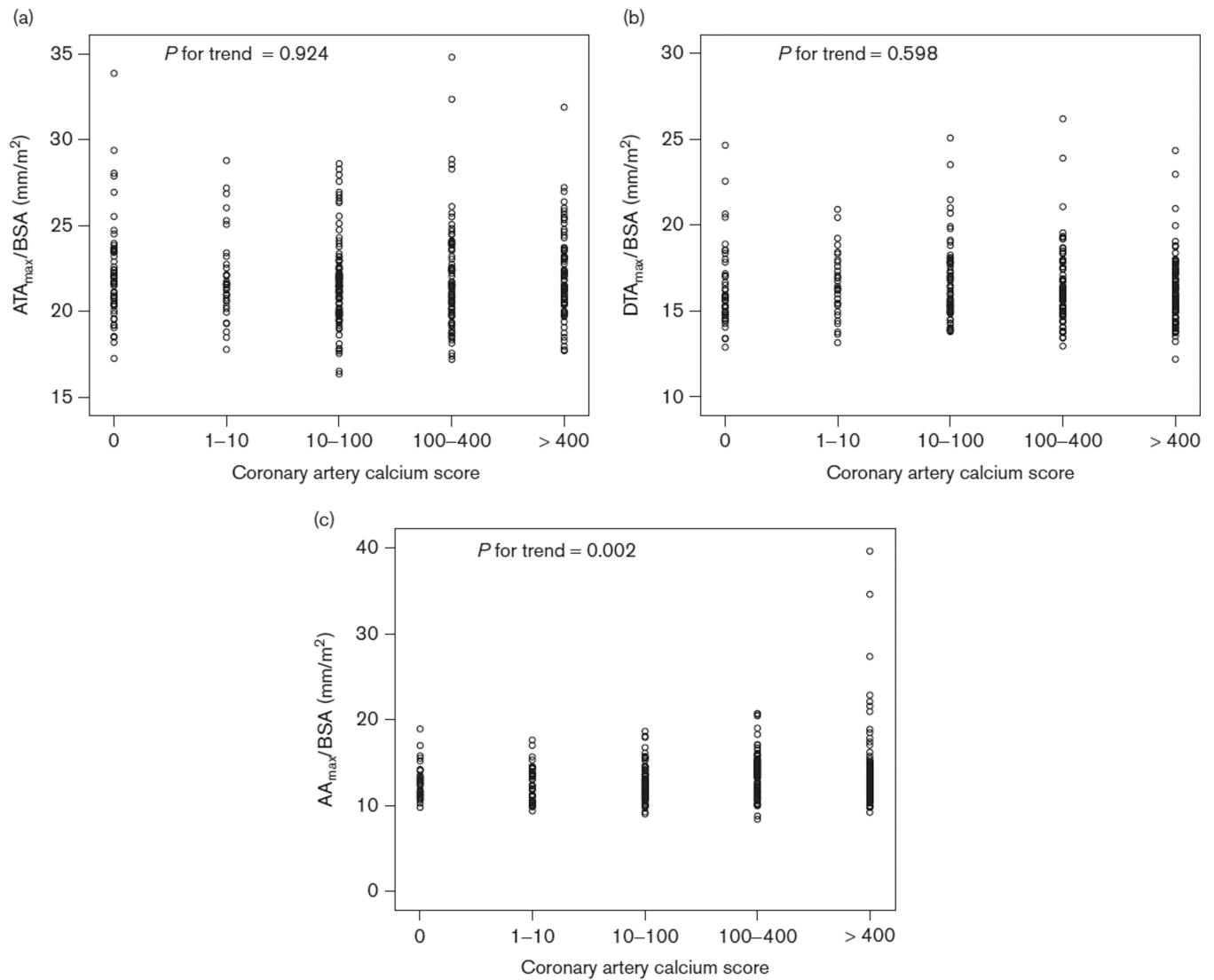


Fig. 2. Correlation between aortic diameters and coronary artery calcium score: (a) ascending thoracic aorta, (b) descending thoracic aorta, and (c) abdominal aorta. ATA_{max} , maximal ascending thoracic aorta diameter; AA_{max} , maximal abdominal aorta diameter; BSA, body surface area; DTA_{max} , maximal descending thoracic aorta diameter.

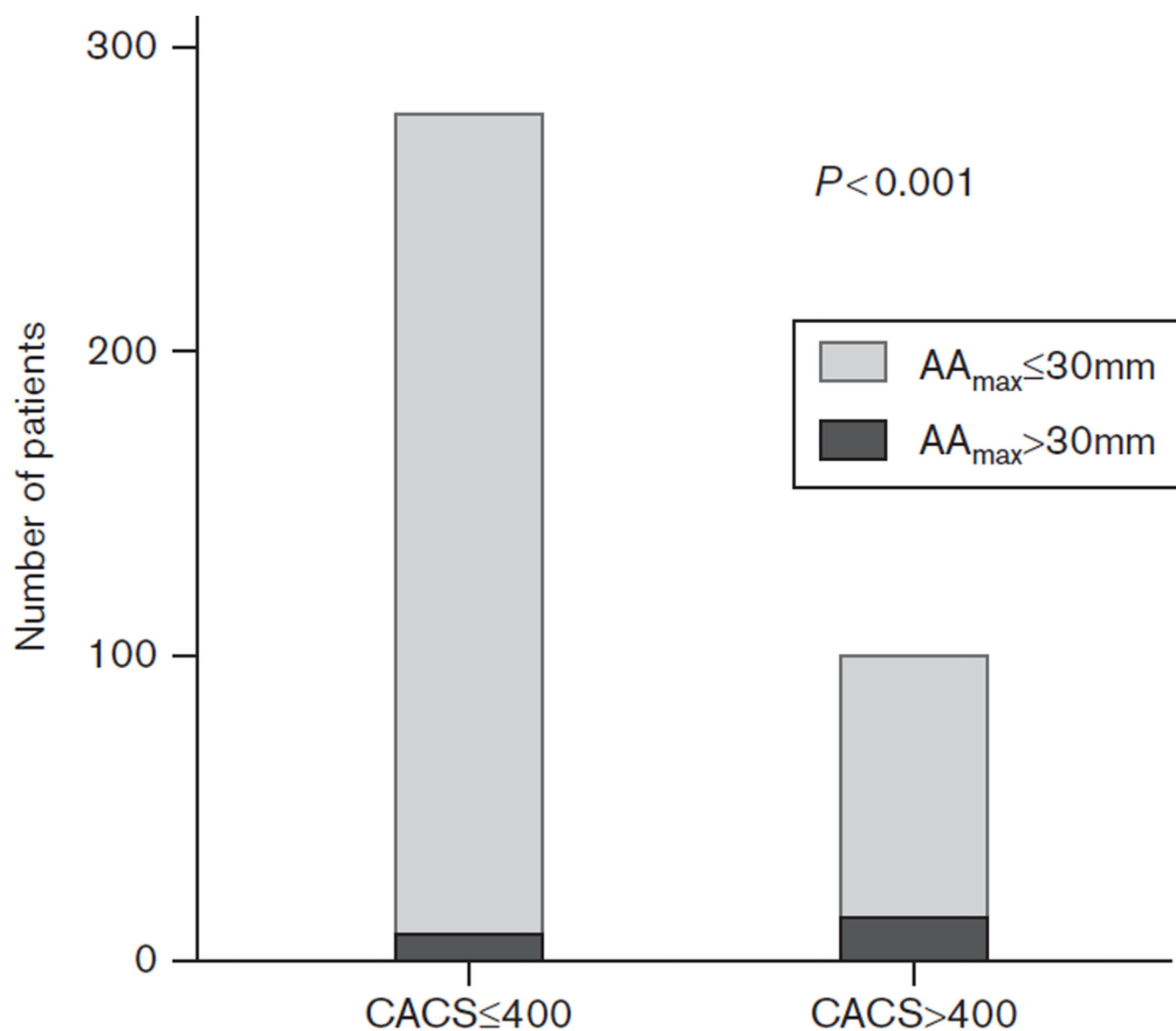


Fig. 3. Prevalence of abdominal aortic (AA) aneurysm according to coronary artery calcium score (CACS).

Table 1

Clinical characteristics of the study population

Variables	Value (n = 393)
Age (years)	73 ± 5
Male [n (%)]	393 (100)
Height (cm)	166.6 ± 7.5
Weight (kg)	67.2 ± 9.4
BSA (m ²)	1.76 ± 0.14
Systolic blood pressure (mmHg)	126 ± 15
Diastolic blood pressure (mmHg)	74 ± 10
Hypertension [n (%)]	393 (100)
Diabetes mellitus [n (%)]	118 (30.0)
Dyslipidemia [n (%)]	229 (58.3)
Ever smoked [n (%)]	277 (70.5)
Aortic valve replacement [n (%)]	15 (3.8)
Medications [n (%)]	
Diuretics	100 (25.4)
β-Blocker	161 (41.0)
ACEi/ARB	280 (71.3)
Calcium channel blocker	724 (61.8)
Laboratory findings (g/ml)	
Calcium	9.0 ± 0.4
Phosphorus	3.4 ± 0.6
Creatinine	1.2 ± 1.1
Total cholesterol	154.1 ± 31.6
LDL-cholesterol	90.6 ± 28.9
HDL-cholesterol	44.2 ± 11.4

ACEi, angiotensin-converting enzyme inhibitor; ARB, aldosterone receptor blocker; BSA, body surface area; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 2

Measurement of aortic diameters according to coronary artery calcium score

Variables	Coronary artery calcium score						P for trend
	0 (n = 56)	1–10 (n = 38)	10–100 (n = 88)	100–400 (n = 107)	>400 (n = 103)		
ATA _{PAB} /BSA (mm/m ²)	22.2 ± 3.2	21.7 ± 2.5	22.0 ± 2.7	21.9 ± 2.8	22.2 ± 2.4		0.901
ATA _{max} /BSA (mm/m ²)	22.2 ± 3.2	21.7 ± 2.5	22.0 ± 2.7	21.9 ± 2.8	22.2 ± 2.4		0.924
DTA _{PAB} /BSA (mm/m ²)	16.0 ± 1.9	16.4 ± 1.8	16.1 ± 1.6	16.0 ± 1.5	16.1 ± 1.4		0.711
DTA _{max} /BSA (mm/m ²)	16.3 ± 2.2	16.5 ± 1.8	16.5 ± 2.0	16.2 ± 2.0	16.3 ± 1.8		0.598
AA _{SMA} /BSA (mm/m ²)	11.7 ± 1.3	12.1 ± 1.6	12.2 ± 1.7	12.0 ± 1.7	12.5 ± 1.8		0.017
AA _{max} /BSA (mm/m ²)	12.5 ± 1.8	12.5 ± 2.0	12.7 ± 2.1	12.9 ± 2.3	13.8 ± 4.5		0.002

AA_{max}, maximal abdominal aorta diameter; AA_{SMA}, abdominal aorta diameter at superior mesenteric artery; ATA_{max}, maximal ascending thoracic aorta diameter; ATA_{PAB}, ascending thoracic aorta diameter at pulmonary artery bifurcation; BSA, body surface area; DTA_{max}, maximal descending thoracic aorta diameter; DTA_{PAB}, descending thoracic aorta diameter at pulmonary artery bifurcation.

Table 3

Linear regression analysis of variables as determinants of maximal aortic diameters

Variables	Univariate		Multivariate	
	β	P-value	β	P-value
ATA _{max} /BSA				
Age	0.203	< 0.001	0.196	< 0.001
Diabetes mellitus	− 0.137	< 0.001	− 0.177	< 0.001
Dyslipidemia	− 1.937	0.053	− 0.069	0.146
AVR	0.221	< 0.001	0.199	< 0.001
Ever-smoking	− 0.058	0.256	−	−
CACS	0.005	0.924	−	−
DTA _{max} /BSA				
Age	0.249	< 0.001	0.244	< 0.001
Diabetes mellitus	− 0.082	0.104	− 0.076	0.120
Dyslipidemia	− 0.089	0.079	− 0.067	0.170
AVR	0.049	0.022	0.093	0.055
Ever-smoking	0.018	0.722	−	−
CACS	− 0.027	0.598	−	−
AA _{max} /BSA				
Age	0.102	0.043	0.149	0.003
Diabetes mellitus	− 0.026	0.614	−	−
Dyslipidemia	0.030	0.550	−	−
AVR	0.008	0.869	−	−
Ever-smoking	0.127	0.013	0.118	0.019
CACS	0.189	0.003	0.125	0.014

AA_{max}, maximal abdominal aorta diameter; ATA_{max}, maximal ascending thoracic aorta diameter; AVR, aortic valve replacement; BSA, body surface area; CACS, coronary artery calcium score; DTA_{max}, maximal descending thoracic aorta diameter.